# Angiotensin Antagonists and Steroids in the Treatment of Focal Segmental Glomerulosclerosis

By Stephen M. Korbet

**The use of angiotensin converting enzyme inhibitors (ACEIs) along with good blood pressure control have been shown to significantly decrease the level of proteinuria and slow the progression of renal insufficiency in patients with nondiabetic glomerular disease including focal segmental glomerulosclerosis (FSGS). Thus, this should be part of the therapeutic approach for all proteinuric patients with FSGS and should be considered the mainstay of therapy for patients with FSGS secondary to conditions associated with hyperfiltration and/or reduced nephron mass and those patients with nonnephrotic primary FSGS. However, nephrotic patients with primary FSGS may continue to have marked proteinuria and progression of renal disease despite these measures and thus require a more aggressive approach with the use of steroids and immunosuppressive agents. Although primary FSGS was once thought to be a steroid-nonresponsive lesion, recent experience has provided a note of optimism in the use of steroids and immunosuppressive agents in treating this otherwise progressive glomerulopathy. As a result, a course of steroid therapy in primary FSGS is now warranted in nephrotic patients with reasonably well preserved renal function in whom it is not otherwise contraindicated.**


PRIMARY FOCAL SEGMENTAL glomerulosclerosis (FSGS) accounts for 7% of glomerular lesions in children and up to 35% of lesions in adults presenting with nephrotic syndrome.[1-9] The prevalence of primary FSGS in black patients is 2 to 4 times that in white patients, being seen in up to 60% of black patients versus 20% of white patients with idiopathic nephrotic syndrome.[5,7,8,10-12] Although the pathogenesis of primary FSGS is unknown, it is well recognized that a similar pattern of injury can be seen in a number of settings with a clinical presentation indistinguishable from primary FSGS.[13,14] Because the pathogenesis and treatment of these disorders may differ significantly, secondary conditions associated with FSGS such as conditions associated with reduced nephron mass and/or hyperfiltration, and infection with human immunodeficiency virus as well as familial forms of FSGS, must be excluded before making the diagnosis of primary FSGS.

Because of the progressive nature of this lesion and the high recurrence rate in transplanted kidneys, often resulting in graft failure, the therapeutic approach to patients with primary FSGS has been of increasing interest to nephrologists.[15] Historically, nephrotic patients with primary FSGS were considered highly steroid unresponsive. However, over the past 20 years an expanding literature has emerged that shows a significant increase in response with an aggressive course of steroid therapy and an improved renal survival for patients attaining a remission. Thus, the prognosis for patients with primary FSGS has become more optimistic. Nonetheless, there remains appropriate concern regarding the potential risks for steroid therapy and questions regarding the possibility that alternate therapies, such as angiotensin converting enzyme inhibitors (ACEIs), may be equally or more effective and associated with less toxicity are being raised.

## CLINICAL PRESENTATION AND COURSE OF PRIMARY FSGS

The presenting feature in all patients with primary FSGS is proteinuria, frequently resulting in the nephrotic syndrome, but a nonnephrotic presentation is not unusual in up to 25% of adults.[16,17] In addition, microscopic hematuria, hypertension, and renal insufficiency are common presenting features. The presentation for patients with primary FSGS may differ among the histologic variants. In contrast to patients with classic FSGS, patients with the cellular or collapsing lesion are more often black, have more advanced renal insufficiency, and more severe proteinuria at presentation.[16,18-21] Massive proteinuria (>10 g/d) at presentation is much more common among patients with the cellular lesion compared with patients with classic FSGS (70% versus 10% of patients).

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The degree of proteinuria at presentation is one of the most important prognostic features in patients with primary FSGS.[4,22-26] Nephrotic patients with primary FSGS reach end-stage renal disease (ESRD) over 5 to 10 years,[4,23-26] and those patients with massive proteinuria (>10 g/24 h) have an even more malignant course with essentially all patients progressing to ESRD within 5 years.[23,27] This is in contrast to the more favorable prognosis in patients with nonnephrotic proteinuria in whom a renal survival of over 80% is observed after 10 years.[4,23-26] Additionally, the level of serum creatinine at presentation is prognostic with patients having a serum creatinine level greater than 1.3 mg/dL manifesting a significantly poorer renal survival than those with a level of 1.3 mg/dL or less.[7,22,24,26,28] Of the various pathologic features that have been studied, the histologic feature that has most consistently been predictive of a poor prognosis is the presence of advanced (>20%) interstitial fibrosis.[16,26,29,30] Recent studies have now shown the presence of the cellular lesion is associated with a significantly more rapid course to ESRD than that of classic FSGS.[6,16,18,19,21,31,32]

## CLINICAL PRESENTATION AND COURSE OF SECONDARY FSGS

The presentation and course of patients with FSGS secondary to conditions resulting from hyperfiltration or functional adaptations such as reflux nephropathy or morbid obesity may differ somewhat from that of primary FSGS. Unlike patients with primary FSGS, those with secondary FSGS often present with a more indolent course and rarely have hypoalbuminemia and nephrotic syndrome despite having nephrotic range or even massive proteinuria.[33,34] In a series of 71 patients with obesity-related FSGS, Kambham et al[33] found that though 47% of obese patients presented with nephrotic range proteinuria only 7% had nephrotic syndrome compared with patients with primary FSGS in whom 66% of patients had nephrotic range proteinuria and 54% had nephrotic syndrome. On renal biopsy examination, patients with FSGS caused by obesity, as well as those caused by reduced nephron mass, reflux nephropathy, or sickle cell disease, were found to have glomerulomegaly (over 30% greater diameter) and less extensive foot process fusion than those patients with primary FSGS.[33-36] Finally, despite similar degrees of renal insufficiency at presentation, patients with secondary FSGS have a less rapidly progressive course with a 5-year renal survival of approximately 80% compared with 50% for patients with primary FSGS.[34,35]

## REMISSION

In primary FSGS, remission of proteinuria best predicts a favorable outcome in nephrotic patients.[16,26,30,37,38] Less than 15% of patients entering a complete remission progress to ESRD, whereas up to 50% of persistently nephrotic patients progress to ESRD over 5 years (Table 1). Even a partial remission is associated with a less rapid decline in renal function as compared with patients in whom the nephrotic syndrome persists.[22,39,40] Unfortunately, spontaneous remissions are rare, occurring in less than 5% of nephrotic patients with primary FSGS.[16,38] However, patients receiving a course of treatment with steroids are 4 to 10 times more likely to enter a remission than untreated patients.[16,30] Because no clinical or histologic feature at presentation allows one to predict which patients will enter a remission, the response to a course of treatment becomes the best clinical indicator of outcome.[16,37,41]

## RESPONSE TO THERAPY WITH ACEIs

The use of ACEIs, and more recently angiotensin II receptor blockers (ARBs), and blood pressure control (≤125/75 mm Hg for proteinuria >1 g/d, and <130/80 mm Hg for proteinuria of 0.25-1 g/d) are now well known to significantly reduce the level of proteinuria and the progression of renal insufficiency in patients with nondiabetic renal disease including primary glomerulopathies.[42-49] Although the benefit of these therapies is seen at all levels of proteinuria, the effect is greatest in those patients with nephrotic range or massive proteinuria.[42,43] Studies comparing the use of ACEI with

**Table 1. Prognosis According to Response to Treatment in Primary FSGS**

| | Patients Progressing to ESRD | | |
|---|---|---|---|
| | Complete Remission | Partial Remission | No Response |
| Adults | 1.7% | 13% | 54% |
| Children | 14% | 0% | 37% |

Data from references 1, 4, 16, 25, 28, 37-39, 57, 65, 66, 69, 73, 75-82.

ARBs in proteinuric patients with immunoglobulin A nephropathy have shown a similar reduction in proteinuria from baseline for both ACEI (61%) and ARB (55%) after 4 weeks of therapy.[49,50] Recently, is has also been shown that there is an additive effect in reducing proteinuria with the combined use of ARBs and ACEI and one may speculate that this would result in further renoprotection.[51-53]

Experience with the use of ACEI alone in patients with primary FSGS is extremely limited. Although the use of ACEI in nephrotic patients with primary FSGS has resulted in a reduction in proteinuria, this has not resulted in a complete remission and, more importantly, this has not been associated with a significant reduction in the rate of progression of renal disease in most studies.[46,54,55] In 5 nephrotic patients with FSGS, Praga et al[46] found that proteinuria decreased by an average of 25% from baseline (10 to 8 g/d) on captopril but, despite this, renal function continued to deteriorate at a rate similar to that before treatment. The use of ACEIs in a slightly larger series of nephrotic patients (22 patients) with primary FSGS[55] again showed a significant reduction in proteinuria with a partial remission being attained in 50% of patients but no patients entered a complete remission. Furthermore, over 2 years of follow-up evaluation there was no improvement in the rate of progression of renal disease because the average serum creatinine level doubled overall with 23% of patients progressing to ESRD.[55]

The use of ACEIs in patients with FSGS secondary to obesity, reflux nephropathy, reduced nephron mass, or sickle cell disease has been associated with a somewhat more optimistic experience.[35,36,46,56] Praga et al[46] found that proteinuric patients with reflux nephropathy and reduced nephron mass had a greater than 50% reduction in proteinuria with captopril and this resulted in a significant reduction in the rate of loss of renal function with a stabilization of serum creatinine levels. Similar beneficial results with the use of ACEIs in FSGS secondary to obesity also have been observed.[33,56] Additionally, marked weight loss (>10% decrease in body mass index) has resulted in a reduction in proteinuria of greater than 50% and stable renal function in obese patients with FSGS.[33,56] Finally, Falk et al[36] observed a 57% reduction in proteinuria in patients with sickle cell nephropathy treated with ACEI.

The beneficial effects of ACEIs (and ARBs) along with good blood pressure control are well established in patients with nondiabetic renal disease overall. In patients with FSGS, the benefit of this therapeutic approach has best been established in secondary forms resulting from hyperfiltration or hemodynamic adaptations. Although one would suspect that this therapy would also be beneficial in patients with primary FSGS, the very limited experience has not been optimistic. Prospective studies are needed in larger numbers of patients with primary FSGS to examine this issue further. Because ACEIs and blood pressure control alone rarely result in a complete remission in nephrotic patients with primary FSGS, nephrologists must pursue the use of immunosuppressive therapies, and this often starts with the use of steroids.

## STEROID THERAPY IN NEPHROTIC CHILDREN

The initial treatment for primary FSGS in children consists of prednisone 60 mg/d/m$^2$ (up to 80 mg/d) given in divided doses for 4 weeks followed by 40 mg/d/m$^2$ (up to 60 mg/d) given in divided doses, 3 consecutive days out of 7, for 4 weeks and then discontinued.[2,57] Although this protocol has been found to be satisfactory for the treatment of children with minimal change disease, it may be inadequate for primary FSGS. The complete remission rate for children with primary FSGS using this treatment protocol has been disappointing at less than 30% in over 80% of patients (Table 2). With the use of a more prolonged course of steroid treatment, Pei et al[37] and Cattran and Rao[38] reported a complete remission in 44% of children with primary FSGS. The median dose of prednisone per treatment course (6 mo) was 120 mg/kg (0.3-2.0 mg/kg/d). The median time to remission was 3 months with patients entering a remission doing so within 6 months of initiating therapy. In one half of patients, a 2-month course of cytotoxic agents were used in addition to prednisone. The renal survival for those patients with a complete remission was 100% at 15 years compared with 73%, 58%, and 51% at 5, 10, and 15 years, respectively, in patients who failed to respond.[37,58] Fifty percent of unresponsive patients had doubling in their serum creatinine levels by 4 years. Based on these findings, they recommended that nephrotic patients with primary FSGS be treated with a course of steroids for up to 6 months.

**Table 2. Response to Initial Treatment in Children**

| Study | Year | n | Complete Remission | Partial Remission | No Response |
|---|---|---|---|---|---|
| White[83] | 1970 | 12 | 17% | 0 | 83% |
| Habib[1] | 1971 | 46 | 20% | 13% | 67% |
| Hyman[77] | 1974 | 13 | 0 | 0 | 100% |
| Nash[84] | 1976 | 20 | 10% | 0 | 90% |
| Newman[80] | 1976 | 16 | 19% | 38% | 43% |
| Mongeau[85] | 1981 | 23 | 26% | 4% | 70% |
| ISKDC[2] | 1981 | 37 | 30% | 0 | 70% |
| Arbus[76] | 1982 | 51 | 51% | 0 | 49% |
| SWPNG[3] | 1985 | 38 | 24% | 0 | 76% |
| Yoshikawa[57] | 1986 | 45 | 18% | 0 | 82% |
| Pei[37] | 1987 | 34 | 44% | 0 | 56% |
| Morita[86] | 1990 | 43 | 12% | 0 | 88% |
| Cattran[38] | 1998 | 32 | 47% | 0 | 53% |
| Frishberg[87] | 1998 | 47 | 30% | 0 | 70% |

Abbreviations: ISKDC, International Study of Kidney Disease in Children; SWPNG, Southwest Pediatric Nephrology Group.

Recently, an extremely aggressive protocol using pulse methylprednisolone and oral steroids has been advocated in children with FSGS resistant to the standard course of steroid therapy (Table 3). Although remission rates of greater than 60% have been reported by Mendoza et al[59] and Tune et al[60] in uncontrolled trials, the same degree of success with this therapy has not been experienced by others (Table 4). The differences in remission rates noted among studies have been attributed to variations in methylprednisolone protocol and the proportion of patients treated with alkylating agents (Table 4).[61,62] Thus, though it appears that improved response rates are attainable with a more prolonged initial course of steroids in children with primary FSGS, the optimal dose and duration of therapy have not been defined.

## STEROID THERAPY IN NEPHROTIC ADULTS

Based on the early and largely disappointing experience with steroid therapy in nephrotic adults with primary FSGS (Table 5), it is not surprising that nephrologists have been less than enthusiastic or even reluctant to subject their adult patients with primary FSGS to a course of steroids or immunosuppressive therapy.[63] Pei et al[37] found that only 42% of nephrotic adults with primary FSGS received treatment as compared with 95% of children. However, over the past 20 years a more optimistic experience has emerged (Table 5) with complete remission rates in excess of 30% being reported in over 80% of studies, with the majority showing complete remission rates of 40% or greater. Insight into the marked differences in re-

**Table 3. Methylprednisolone Protocol for Children With FSGS**

| Week | Methylprednisolone* | Prednisone† | Cytotoxic Therapy |
|---|---|---|---|
| 1-2 | 30 mg/kg, 3 × wk | None | None |
| 3-10 | 30 mg/kg, every 1 wk | 2 mg/kg every other day | None |
| 11-18 | 30 mg/kg, every 2 wk | 2 mg/kg every other day | ‡ |
| 19-52 | 30 mg/kg, every 4 wk | 2 mg/kg every other day | None |
| 53-78 | 30 mg/kg, every 8 wk | 2 mg/kg every other day | None |

* Up to 1,000 mg per dose.

† Up to 60 mg

‡ At week 11, patients who are considered treatment failures are given either cyclophosphamide 2 mg/kg/d or chlorambucil 0.2 mg/kg/d for 8 to 12 weeks.

Data from Mendoza et al.[59,60]

**Table 4. Response to Pulse Methylprednisolone and Cytotoxic Therapy**

| Study | n | Remission | Cytotoxic Therapy* |
|---|---|---|---|
| Tune[62] | 11 | 72% | 100% |
| Tune[60] | 32 | 75% | 78% |
| Aviles[88] | 5 | 60% | 60% |
| Guillot[74] | 15 | 54% | 53% |
| Waldo[89] | 10 | 0 | 20% |

* Proportion of patients treated with cytotoxic therapy.

mission rates can be obtained by comparing the treatment protocols used (Table 6). The most obvious difference among studies was the duration of therapy because the initial dose of prednisone used was similar. The total duration of therapy in those studies with a poor response rate was 2 months or less (low-dose therapy) compared with an average of 5 to 9 months (high-dose therapy) in studies achieving high remission rates (Table 6). Ponticelli et al[30] reported a complete remission in only 15% of patients treated with steroids for less than 4 months, whereas 61% of patients treated for 4 months or more entered a complete remission. The initial period of daily, high-dose steroids also may be an important factor. In most studies achieving high complete remission rates, the duration of high-dose steroids was maintained for 2 to 3 months before tapering. Rydel et al[26] found that, in addition to a longer overall course of treatment (5 versus 3 mo), those patients achieving a remission had received an initial period of high-dose prednisone ($\geq$60 mg/d) for a significantly longer duration than nonresponders (median time of 3 versus 1 mo, respectively). Thus, the initial duration of high-dose treatment may be as important as the overall duration of therapy.

Less than one third of adults who achieve a complete remission do so by 8 weeks of therapy. The median time to complete remission is 3 to 4 months, with the majority of patients reaching a complete remission by 5 to 9 months from the beginning of treatment.[24,26,37-39] Based on this experience, it has now been proposed that steroid resistance in adults be defined as the persistence of the nephrotic syndrome after a 4-month trial of therapy with prednisone at a dose of 1 mg/kg/d.[64]

Although the presence of the cellular lesion generally has been associated with a poor therapeutic response, with remissions in less than 20% of treated patients,[18,19,31,32] we have observed no dif-

**Table 5. Response to Initial Treatment in Adults**

| Study | Year | n | Complete Remission | Partial Remission | No Response |
|---|---|---|---|---|---|
| Lim[79] | 1974 | 10 | 0 | 10% | 90% |
| Jenis[78] | 1974 | 6 | 0 | 33% | 67% |
| Velsoa[82] | 1975 | 34 | 12% | 29% | 59% |
| Saint-Hillier[69] | 1975 | 23 | 70% | 0 | 30% |
| Newman[80] | 1976 | 8 | 0 | 50% | 50% |
| Bolton[65] | 1977 | 10 | 0 | 40% | 60% |
| Cameron[25] | 1978 | 20 | 10% | 0 | 90% |
| Beaufils[4] | 1978 | 26 | 19% | 31% | 50% |
| Korbet[24] | 1986 | 16 | 31% | 19% | 50% |
| Miyata[90] | 1986 | 32 | 44% | 12% | 44% |
| Pei[37] | 1987 | 18 | 39% | 0 | 61% |
| Chan[28] | 1991 | 13 | 23% | 31% | 46% |
| Banfi[39] | 1991 | 59 | 61% | 0 | 39% |
| Agarwal[75] | 1993 | 38 | 32% | 26% | 42% |
| Nagai[66] | 1994 | 9 | 44% | 11% | 44% |
| Rydel[26] | 1995 | 30 | 33% | 17% | 50% |
| Shiiki[81] | 1996 | 35 | 34% | 31% | 34% |
| Cattran[38] | 1998 | 17 | 47% | 0 | 53% |
| Ponticelli[30] | 1999 | 80 | 36% | 16% | 48% |
| Schwartz[16] | 1999 | 42 | 33% | 19% | 48% |
| Alexopoulos[73] | 2000 | 11 | 28% | 36% | 36% |

**Table 6. Initial Steroid Treatment in Adults With FSGS**

| Response | Dose (mg/kg/d) | High-dose Duration (mo) | Total Duration (mo) |
|---|---|---|---|
| Low dose | | | |
| Lim[79] | 0.5–1.5 | | 2 |
| Velosa[82] | 0.5–1.0 | 1 | 2 |
| Beaufils[4] | 1.0–1.5 | 1 | 3 |
| High dose | | | |
| St. Hillier[69] | 0.5–1.5 | 3 | 6–12 |
| Korbet[16,24,26] | 0.5–1.0 | 2–3 | 6–8 |
| Pei[37, 38] | 0.3–2.0 | | 8 |
| Banfi[30,39] | 0.5–1.0 | 2 | 6–9 |
| Agarwal[75] | 1.0 | 2–3 | 6 |
| Shiiki[81] | 0.5–1.0 | 1–2 | 36 |
| Alexopoulos[73] | 1.0 | >1 | 24 |

ference in the remission rate for patients with cellular FSGS compared with patients with classic FSGS. We found that a remission was achieved in 52% of patients (complete 32% and partial 20%) with cellular FSGS and 53% of patients (complete 35% and partial 18%) with classic FSGS.[16] However, we too found the remission rate was only 23% in those patients whose biopsy examinations showed greater than 20% involvement of glomeruli with cellular lesions.[16] The reason for the different response rates among studies is not clear but may relate to differences in therapeutic approach or the presence of more advanced renal disease at biopsy examination in those studies experiencing a poor response.[18-21]

The use of alternate-day steroid therapy in primary FSGS has been considered to minimize the potential for complications associated with daily steroid use, particularly in older adults. To date, however, the response to alternate-day steroids has been disappointing in young adults.[65] Of 10 young adult patients treated by Bolton et al[65] with 60 to 120 mg of prednisone every other day for 9 to 12 months, none sustained a complete remission. However, Nagai et al[66] attained a complete remission in 5 (44%) of 9 nephrotic patients greater than 60 years of age by using 1.0 to 1.6 mg/kg (up to 100 mg) every other day for 3 to 5 months. After 3 years of follow-up evaluation, no relapses occurred and no patient with a complete remission progressed to ESRD compared with 47% of untreated or nonresponsive patients. The therapy was well tolerated without obvious complication. The excellent response rate with alternate-day steroid therapy in the elderly may be owing to the significant decrease in clearance of steroids observed in the elderly, leading to a higher relative serum concentration of steroid and/or a more sustained steroid effect.[67,68]

Cytotoxic agents along with steroids have been used as initial therapy in approximately 20% of adults, but this appears to confer no added benefit in attaining a complete remission when compared with steroids alone (Table 7).[30,39] However, their use may induce a more stable remission than steroids alone.[30,39,69] Ponticelli et al[30] and Banfi et al[39] observed a relapse rate of only 18% in patients initially receiving cytotoxic agents along with steroids compared with 55% of patients relapsing when treated with steroid alone. Ultimately, the percent of patients in complete remission (47% versus 59%, respectively) was not significantly different between the 2 groups.

The prognosis for nephrotic FSGS patients who are steroid resistant is quite poor in general (Table 1). In this setting, the use of alternative immunosuppressive therapies such as cytotoxic agents and calcineurin inhibitors have been used with limited success.[17]

## STEROID THERAPY IN NONNEPHROTIC AND SECONDARY FSGS

There are essentially no data regarding the use and/or benefit of steroids in nonnephrotic patients with primary FSGS. Owing to the more favorable course in these patients we take a more conservative approach and avoid steroids, considering them only if the patient becomes nephrotic. Familial forms of FSGS are known to be steroid resistant and thus, steroids are of little value in these patients.[70,71] In patients with secondary FSGS caused by hyperfiltration and/or reduced nephron mass (especially in patients with obesity), it also is our

**Table 7. Initial Treatment in Adults**

| Treatment | n | Complete Remission | Partial Remission | No Response |
|---|---|---|---|---|
| Steroids alone | 420 | 35% | 19% | 46% |
| Steroids with cytotoxics | 117 | 31% | 11% | 58% |

Data from references 4, 16, 24-26, 28, 30, 37, 39, 65, 66, 69, 73, 75, 78-82, 90.

feeling that steroids have no place in the management of these patients and should be avoided because the risk would be greater than any potential benefit. Additionally, they may exacerbate the underlying disease (particularly in obesity-related FSGS) and accelerate the progression of renal disease. However, obese patients suspected of having primary FSGS, owing to the sudden onset of nephrotic syndrome, have been treated with steroid therapy with good response.[33]

## COMPLICATIONS OF STEROID THERAPY

The use of prolonged courses of steroids raise appropriate concern regarding potential side effects in children and adults alike. Although significant side effects from the high-dose and prolonged courses of steroid therapy used have not been routinely encountered even in studies with average treatment durations of up to 9 months, one must be cautious because the retrospective nature of most studies makes it difficult to accurately track and assess for side effects.[2,16,24,26,30,37,39,66,69,72,73] A Cushingoid appearance is the most common complication reported, seen in up to 33% of cases, though proximal myopathy (16%), hypertension (5%), gastric discomfort (5%), and diabetes mellitus (2% to 5%) occur less frequently.[30,73] Severe side effects, though infrequently observed, usually have been encountered in the setting of combined treatment with cytotoxic agents or cyclosporin A.[30,38]

In children, the prolonged course of high-dose intravenous methylprednisolone has not been without its cost. The development of cataracts (22%), hypertension (17%), slowed growth (17%), leukopenia (19%), and infectious complications (17%) were not infrequent in patients treated by Mendoza et al.[59] In another study, the use of pulse steroid therapy lead to sepsis in 20% (3 of 15) of children treated, leading to the death of one patient.[74]

## RECOMMENDATIONS

The use of ACEIs (or ARBs) along with good blood pressure control should be part of the therapeutic approach for all proteinuric patients with FSGS and should be considered the mainstay of therapy for patients with FSGS secondary to conditions associated with hyperfiltration and/or reduced nephron mass and those patients with nonnephrotic primary FSGS. For nephrotic patients with primary FSGS, recent experience has provided a note of optimism in the use of immunosuppressive agents in treating this otherwise progressive glomerulopathy. As a result, a course of steroid therapy in primary FSGS is warranted in nephrotic patients with reasonably well preserved renal function (serum creatinine levels $\leq$3 mg/dL) in whom it is not otherwise contraindicated. As an initial approach to treatment in adults, prednisone is given at a dose of 1 mg/kg/d (up to 80 mg) for 3 to 4 months. In the elderly ($\geq$60 y), an initial alternate-day regimen of prednisone (1-2 mg/kg up to 120 mg) for 4 to 5 months may be prudent. In patients showing a response to treatment (ie, a remission or a $\geq$50% reduction in proteinuria), the dose can be slowly tapered over an additional 3 months. For patients unresponsive to the initial course of therapy, a more rapid taper, over 4 weeks, should be used to minimize further steroid exposure. Steroids should be avoided in patients with familial FSGS or FSGS secondary to hyperfiltration and/or reduced nephron mass.

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